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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Our Ref: 1038-588 MIS:as

RECEIVED

In re patent application

No. 08/634,039
Applicant: Denis P. Snider
Title: METHODS AND COMPOSITIONS CONTAINING
ANTIGENS HAVING A TARGETING MOIETY SPECIFIC
FOR ANTIGEN PRESENTING CELLS FOR
INTRANASAL IMMUNIZATION

JUN 25 1999

**MATRIX CUSTOMER
SERVICE CENTER**



Filed: April 17, 1996
Group No. 1644
Examiner: F. VanderVegt

June 21, 1999

BY COURIER

The Commissioner of Patents
and Trademarks,
Washington, D.C. 20231,
U.S.A.

Handwritten notes:
- 11/11/98 (3-m)
- Extension of 3 months
- 7/7/98
- 1/1/99

Dear Sir:

This Communication is in response to the Office Action of December 23, 1998.

Petition is hereby made under the provisions of 37 CFR 1.136(a) for an extension of three months of the period for response to the outstanding Office Action on this case. We enclose our cheque in the amount of the prescribed fees.

The Examiner questioned the intent of the Petition to Correct Inventorship. The intent is to correct the inventorship. When the application was filed, there was submitted an unexecuted Declaration and Power of Attorney (copy enclosed) naming Denis P. Snider, Brian J. Underdown and Mark R. McDermott as joint inventors. It was appreciated shortly after the filing that there was a single inventor only, Denis P. Snider.

In response to the Notice to File Missing Parts, there was submitted, by our letter of November 6, 1996, a Declaration and Power of Attorney signed by the inventor Snider alone, along with a promise to file the Petition to Correct

Inventorship. That promise was fulfilled by our letter of November 22, 1996, referencing the November 6, 1996 letter. No action has apparently been taken on the Petition, but the Office issued a filing receipt indicating Dennis P. Snider as the sole inventor.

However, having regard to the submission of an unexecuted Declaration and Power of Attorney with three named inventors, it is believed necessary to correct the record, so as to explain the apparent discrepancy between the unexecuted paper originally filed and the executed paper.

Having regard to the Examiner's comments concerning the actual documentation, the Declaration of Mark R. McDermott is clearly at odds with the other documentation. The Declaration should take the same form as that of Brian J. Underdown. A substitute Declaration will follow. In addition, a substitute Declaration and Power of Attorney signed by the sole inventor Denis P. Snider also will follow.

It is believed that the above explanation and the additional documentation to follow clarify the matter.

The Examiner rejected claims 1 to 9 under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As the Examiner notes, applicant's claims are directed to a method of generating an immune response to an antigen in a host by intranasal administration to the host of an antigen coupled to a targeting moiety specific for surface structures of antigen-presenting cells. There has previously been described, in the Barber et al patents cited by the Examiner, the parenteral administration of such antigen-coupled antibody and the enhancement of immunogenicity to the antigens in the absence of conventional adjuvants.

The applicants have pointed to the literature with respect to the production of local secreting IgA and systemic IgG responses and intranasal administration (see p. 2, l.26 to p. 3, l.17). The Examiner's discussion of T-cell response is interesting but irrelevant to the identification of an immune response by IgG or IgA responses, which is what applicants describe and the art has described as a correlation to protection.

Accordingly, applicants claims are fully enabled in this respect.

The Examiner further noted that the applicants had exemplified their invention using hen egg lysozyme. It is, of course, not necessary to exemplify every possible embodiment of an invention for the claims to be enabled. The applicants exemplification using hen egg lysozyme (HEL) demonstrates the principle of using antigen-activity conjugates to obtain an immune response by intranasal administration. As little as 0.1 μ g of HEL, given twice as a component of an immunotargeting conjugate with anti-MHCII IgG2b monoclonal antibody, was sufficient to prime mice for a secondary humoral immune response to HEL. By comparison, very little antibody response was seen in mice immunized with up to 10 μ g of HEL alone. In addition, at an equivalent HEL dose, the targeting conjugate primed mice for greater secondary antibody responses than HEL in the presence of CT, a known strong mucosal adjuvant. While both serum IgG and secreting IgA declined with decreasing dose, specific antibodies in nasal washings remained at relatively high levels even with the lowest dose employed.

While the success in eliciting a good immune response to an antigen by parenteral administration of the antigen-antibody conjugate as described in the Barber et al patents is not predictive of obtaining a strong immune response by intranasal administration of the antigen antibody conjugates, nevertheless, once having demonstrated the principle of obtaining an immune response by intranasal administration, as the applicants have done using HEL, then there is good reason to believe, based on the work described by Barber et al, that the intranasal administration route has generic application to antigens.

Accordingly, it is submitted that the claims are fully enabled and hence the rejection thereof under 35 USC 112, first paragraph, should be withdrawn.

The Examiner rejected claims 1 to 6 and 8 under 35 USC 103 as being unpatentable over Barber et al '480 or Barber et al '254, each in view of Wu et al.

The Examiner is correct that the Barber et al '480 and '252 patents describe a method of conferring protection against pathogenic organisms using monoclonal antibodies specific for membrane determinants expressed on mammalian antigen presenting cells as a targeting moiety, which are coupled to antigens derived from pathogenic organisms. As the Examiner notes, the Barber et al patents do not teach intranasal administration or a heterobifunctional linking molecule.

As to Wu et al, the Examiner observes that the reference teaches nasal administration of *S. mutans* surface protein antigen I/II coupled to cholera toxin B subunit (CTB). The results obtained provide no suggestion that an antigen coupled to a monoclonal antibody could provoke an immune response by nasal administration. CTB is a well-known adjuvant of antigens administered to mucosal surfaces, such as by intranasal immunization. The Barber et al references describe the use of monoclonal antibodies to target antigens to antigen presenting cells by parenteral immunization. There is no suggestion that such a targeting system could be employed for intranasal immunization and hence the art lacks the motivation suggested by the Examiner.

Accordingly, claims 1 to 6 and 8 are patentable over the applied art and hence the rejection thereof under 35 USC 103(a) as being unpatentable over Barber et al U.S. Patent No. 4,950,480 or Barber et al U.S. Patent No. 5,194,254, each in view of Wu et al, should be withdrawn.

The Examiner rejected claim 7 under 35 USC 103(a) as being unpatentable over the Barber et al patents each in view of Wu et al and further in view of Dempsey et al and ATCC Catalogue.

The relevance of the combination of the Barber et al patents each with Wu et al, has been discussed above. It is submitted that the secondary references do not make up the deficiencies of the primary combination of references. As the Examiner points out, Dempsey et al teaches conjugation of antigen to C3d and ATCC catalog offers for sale the hybridoma which produces the anti-human C3d receptor (CD21) Mab THB-5. However, the Dempsey et al conjugate is administered to mice intraperitoneally and hence is no more relevant to the patentability of claim 7 than the Barber et al patents and to the patentability of claim 1, on which claim 7 ultimately depends.

Accordingly, it is submitted that claim 7 is patentable over the art and hence the rejection thereof under 35 USC 103(a) as being unpatentable over the Barber et al patents, each in view of Wu et al, and further in view of Dempsey et al and ATCC catalogue, should be withdrawn.

The Examiner rejected claim 9 under 35 USC 103(a) as being unpatentable over the Barber et al patents each in view of Wu et al and Babington. The Babington reference is relied on for a teaching of a nebulizer which can be used

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to aerosolize medicaments for nasal inhalation and not for any teaching which would serve to remedy the defects of the primary combination of references and as discussed in detail above.

Accordingly, it is submitted that claim 9 is patentable over the art and hence the rejection thereof under 35 USC 103(a) as being unpatentable over the Barber et al patents, each in view of Wu et al and Babington, should be withdrawn.

It is noted that the Examiner has lined through the duplicate reference on the IDS.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,

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